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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/920,342	08/01/2001	Shi-Lung Lin	13761-7024	4134

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EXAMINER	
CHONG, KIMBERLY	
ART UNIT	PAPER NUMBER
1635	
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02/14/2008	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	09/920,342	LIN ET AL.	
	Examiner	Art Unit	
	Kimberly Chong	1635	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *14 May 2007 and 27 November 2007*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *32,34-36,38,40-45,55,58-61 and 63-71* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *32,34-36,38,40-45,55,58-61 and 63-71* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

The previous restriction requirement mailed 08/09/2007 requiring Applicant to elect a target sequence is vacated because the restriction requirement was made in error. The Examiner apologizes for any inconvenience caused this may have caused Applicant.

The target genes drawn to sonic hedgehog and bcl2 added in claims 35, 36, 59 and 60 the amendment filed 05/14/2007 should have been withdrawn as being drawn to a non-elected invention because the Beta-cantenin gene was elected by original presentation given Applicant received several Office actions wherein the Beta-cantenin gene was previously examined and because the Beta-cantenin gene was previously elected in the response to restriction requirement filed 11/16/2003.

Status of Application/Amendment/Claims

Applicant's response filed 05/14/2007 has been considered. Rejections and/or objections not reiterated from the previous office action mailed 01/12/2007 are hereby withdrawn. The following rejections and/or objections are either newly applied or are reiterated and are the only rejections and/or objections presently applied to the instant application. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Claims 32, 34-36, 38, 40-45, 55, 58-61 and 63-71 are pending and currently under examination. Newly submitted target genes Shh and bcl-2 and target genes having SEQ ID Nos. 12, 13, 14 and 15 and blc2 sequence amplified by SEQ ID Nos. 8

and 9 are directed to an invention that is independent or distinct from the invention originally claimed for the following reasons:

Claims 35, 36, 59 and 60 specifically claim target gene sequences comprising a Shh gene or a bcl-2 gene, a region from the sonic hedgehog sequence amplified by SEQ ID NOs. 12, 13, 14 and 15, a B-catenin sequence encoding its amino acid domain from positions 306 to 644 and a bcl-2 sequence amplified by SEQ ID Nos. 8 and 9. Each sequence is considered to be unrelated, since each sequence claimed is structurally and functionally independent and distinct for the following reasons: each of the claimed sequences are unique and therefore would require a different hybrid duplex that would bind to each target sequence independently and modulate expression or each target gene to a different degree. Moreover, each of the claimed sequences do not share a substantial structural feature or a common utility such that a search for a hybrid duplex that binds a target gene comprising SEQ ID No. 12 would yield a hybrid duplex that binds to a target gene comprising a bcl-2 sequence amplified by SEQ ID NO. 8, for example.

Since applicant has received an action on the merits for the originally presented invention e.g. Beta-cantenin target gene, this invention has been constructively elected by original presentation for prosecution on the merits. Accordingly, target genes Shh, bcl2 and target genes having SEQ ID Nos. 12, 13, 14 and 15 and blc2 sequence amplified by SEQ ID Nos. 8 and 9 are withdrawn from consideration as being directed to a non-elected invention. See 37 CFR 1.142(b) and MPEP § 821.03.

Re: Claim Rejections - 35 USC § 112

The rejection of claims 32, 34-36, 38, 40-45, 55, 58-61 and 63-71 under 35 U.S.C. 112, first paragraph, is maintained for the reasons of record in the Office action mailed 1/12/2007.

Applicant's arguments filed 05/14/2007 have been fully considered but they are not persuasive. Applicant has amended the claims to clarify that the gene silencing mechanism of the mRNA-cDNA hybrid duplex goes through the intracellular RNAi mechanism and further to specify a region of the Beta-canenin target sequence. The rejection of record would still apply to these claim amendments.

Applicant argues the unpredictability of the use of RNA-DNA hybrid duplexes taught by Parrish et al. and Tuschl et al. refer to short hybrid duplexes (19-25 base pairs) and do not teach or suggest the present invention which is the use of larger hybrid duplexes of 500 bases pairs or more. Therefore, Applicant argues, the findings of Parrish et al. and Tuschl et al. are irrelevant to the enablement of the present invention. Applicant's arguments are not convincing. Because it is known that longer duplexes are cleaved into shorter duplexes once they enter the cell by Dicer and the short duplexes are responsible for mediating RNAi, the findings of Parrish et al. and Tuschl et al. are still relevant.

Applicant further argues that the hybrid duplex mechanism of the present invention, referred to as D-RNAi, relies on the generation of small microRNA or piRNA rather than siRNA and this gene silencing mechanism functions through a coupled interaction between pol-II-directed pre-mRNA transcription and RNA splicing. Applicant

cites numerous references in support of the presently claimed invention being enabled because the presently claimed invention, as alleged by Applicant, uses the D-RNAi mechanism instead of the siRNA mediated RNAi pathway. In response, the claimed invention is not drawn to a D-RNAi mechanism of RNA interference as argued by Applicant. The presently claimed invention is drawn to a method for inhibiting the expression of a target gene through an intracellular RNA interference mechanism which encompasses RNAi mediated by siRNA and this method using a mRNA-cDNA hybrid duplex to inhibit expression in vivo is not enabled for the reasons of record.

Furthermore, the references cited by Applicant do not provide guidance for claimed breadth of the instant invention. The references cited are drawn to this D-RNAi mechanism, which is not instantly claimed and even if, for the sake of argument, this D-RNAi mechanism was claimed, the references were filed after the filing of the instant invention. The state of the prior art is what one skilled in the art would have known, at the time the application was filed, about the subject matter to which the claimed invention pertains. The relative skill of those in the art refers to the skill of those in the art in relation to the subject matter to which the claimed invention pertains at the time the application was filed. See MPEP § 2164.05(b). The state of the art for a given technology is not static in time. It is entirely possible that a disclosure filed on January 2, 1990, would not have been enabled. However, if the same disclosure had been filed on January 2, 1996, it might have enabled the claims. Therefore, the state of the prior art must be evaluated for each application based on its filing date. 35 U.S.C. 112 requires the specification to be enabling only to a person “skilled in the art to which it pertains, or

with which it is most nearly connected." The state of the art existing at the filing date of the application is used to determine whether a particular disclosure is enabling as of the filing date. > Chiron Corp. v.Genentech Inc., 363 F.3d 1247, 1254, 70 USPQ2d 1321, 1325-26 (Fed. Cir.2004).

Therefore, because there is no guidance in the specification as filed that teaches inhibition of expression of any target gene *in vivo* after administration of a mRNA-cDNA hybrid duplex and because the state of the prior art at the time of filing provides evidence that the use of RNA-DNA hybrid duplex for RNAi was unpredictable, the instantly claimed invention is not described in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

Thus, the rejection of record is maintained.

Conclusion

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of

the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Kimberly Chong whose telephone number is 571-272-3111. The examiner can normally be reached Monday thru Thursday between 6 and 3 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James Schultz can be reached at 571-272-0763. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Patent applicants with problems or questions regarding electronic images that can be viewed in the Patent Application Information Retrieval system (PAIR) can now contact the USPTO's Patent Electronic Business Center (Patent EBC) for assistance. Representatives are available to answer your questions daily from 6 am to midnight (EST). The toll free number is (866) 217-9197. When calling please have your application serial or patent number, the type of document you are having an image problem with, the number of pages and the specific nature of the problem. The Patent Electronic Business Center will notify applicants of the resolution of the problem within 5-7 business days. Applicants can also check PAIR to confirm that the problem has been corrected. The USPTO's Patent Electronic Business Center is a complete service center supporting all patent business on the Internet. The USPTO's PAIR system provides Internet-based access to patent application status and history information. It also enables applicants to view the scanned images of their own application file folder(s) as well as general patent information available to the public. For more information about the PAIR system, see http://pair-direct.uspto.gov.

For all other customer support, please call the USPTO Call Center (UCC) at 800-786-9199.

KC
Art Unit 1635

//Sean R McGarry//

Primary Examiner, Art Unit 1635